

(2) To 0.1 g of Chlorobutanol add 5 mL of sodium hydroxide TS, shake well the mixture, add 3 to 4 drops of aniline, and warm gently: the disagreeable odor of phenyl isocyanide (poisonous) is perceptible.

**Purity (1) Acid**—Shake thoroughly 0.10 g of the powder of Chlorobutanol with 5 mL of water: the solution is neutral.

(2) **Chloride**—Dissolve 0.5 g of Chlorobutanol in 25 mL of dilute ethanol, and add 6 mL of dilute nitric acid and water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution with 1.0 mL of 0.01 mol/L hydrochloric acid VS by adding 25 mL of dilute ethanol, 6 mL of dilute nitric acid and water to make 50 mL (not more than 0.071%).

**Water** Not more than 6.0% (0.2 g, direct titration).

**Residue on ignition** Not more than 0.10% (1 g).

**Assay** Transfer about 0.1 g of Chlorobutanol, accurately weighed, to a 200-mL conical flask, and dissolve in 10 mL of ethanol (95). Add 10 mL of sodium hydroxide TS, boil under a reflux condenser for 10 minutes, cool, add 40 mL of dilute nitric acid and exactly 25 mL of 0.1 mol/L silver nitrate VS, and shake well. Add 3 mL of nitrobenzene, and shake vigorously until the precipitate is coagulated. Titrate the excess silver nitrate with 0.1 mol/L ammonium thiocyanate VS (indicator: 2 mL of ammonium iron (III) sulfate TS). Perform a blank determination.

$$\begin{aligned} &\text{Each mL of 0.1 mol/L silver nitrate VS} \\ &= 5.915 \text{ mg of } \text{C}_4\text{H}_7\text{Cl}_3\text{O} \end{aligned}$$

**Containers and storage** Containers—Tight containers.

## Chlorpheniramine and Calcium Powder

クロルフェニラミン・カルシウム散

Chlorpheniramine and Calcium Powder contains not less than 0.27% and not more than 0.33% of chlorpheniramine maleate ( $\text{C}_{16}\text{H}_{19}\text{ClN}_2 \cdot \text{C}_4\text{H}_4\text{O}_4$ : 390.86).

### Method of preparation

Chlorpheniramine Maleate	3 g
Dibasic Calcium Phosphate	800 g
Starch, Lactose, or their mixture	a sufficient quantity
To make 1000 g	

Prepare as directed under Powders, with the above ingredients.

**Description** Chlorpheniramine and Calcium Powder occurs as a white powder.

**Identification (1)** Determine the absorption spectrum of the sample solution obtained in the Assay: it exhibits a maximum between 263 nm and 267 nm (chlorpheniramine maleate).

(2) To 0.5 g of Chlorpheniramine and Calcium Powder add 10 mL of dilute hydrochloric acid, shake well, and filter: the filtrate responds to the Qualitative Tests (3) for calcium

salt.

(3) To 0.5 g of Chlorpheniramine and Calcium Powder add 10 mL of dilute nitric acid, shake well, and filter: the filtrate responds to the Qualitative tests (2) for phosphate.

(4) Shake 1 g of Chlorpheniramine and Calcium Powder with 5 mL of methanol, filter, and use the filtrate as the sample solution. Separately, dissolve 0.01 g of chlorpheniramine maleate in 17 mL of methanol, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 10  $\mu\text{L}$  each of the sample solution and the standard solution on the plate of silica gel with fluorescent indicator for thin-layer chromatography. Develop the plate with a mixture of chloroform, methanol, acetone and ammonia solution (28) (73:15:10:2) to a distance of about 10 cm. Air-dry the plate, and examine under ultraviolet light (main wavelength: 254 nm): the spots from the sample solution and from the standard solution show the same  $R_f$  value. Spray evenly Dragendorff's TS for spraying upon the plate: the spot from the standard solution and the corresponding spot from the sample solution reveal an orange color.

**Assay** Weigh accurately about 0.5 g of Chlorpheniramine and Calcium Powder, transfer to a 30-mL glass-stoppered centrifuge tube, add 20 mL of 0.05 mol/L sulfuric acid VS, shake for 5 minutes, centrifuge, and collect the supernatant liquid. Add 20 mL of 0.05 mol/L sulfuric acid VS to the residue, and proceed twice in the same manner mentioned above. Transfer all the supernatant liquid to a 200-mL separator, add 30 mL of diethyl ether, shake, and allow to stand for 5 minutes. Filter the water layer through dry filter paper into another separator. Extract the diethyl ether layer with two 10-mL portions of 0.05 mol/L sulfuric acid VS, filter the extracts into the preceding separator containing the water layer. Wash the filter paper with 5 mL of 0.05 mol/L sulfuric acid VS, combine the washings with the water layer in the preceding separator, and add 10 mL of ammonia TS. Extract with two 50-mL portions of diethyl ether, combine the diethyl ether layer, wash with 20 mL of water, and extract the diethyl ether layer with two 20-mL and 5-mL portions of 0.25 mol/L sulfuric acid VS. Combine all the extracts, add 0.25 mol/L sulfuric acid VS to make exactly 50 mL, and use this solution as the sample solution. Separately, dissolve about 0.075 g of chlorpheniramine maleate for assay, previously dried at 105°C for 3 hours and accurately weighed, in 10 mL of 0.05 mol/L sulfuric acid VS, and add 0.05 mol/L sulfuric acid VS to make exactly 100 mL. Pipet 2 mL of the solution into a 200-mL separator, add 58 mL of 0.05 mol/L sulfuric acid VS and 30 mL of diethyl ether, and shake. Proceed in the same manner as the sample solution, and use this solution as the standard solution. Determine the absorbances,  $A_T$  and  $A_S$ , of the sample solution and the standard solution at 265 nm, using 0.25 mol/L sulfuric acid VS as the blank.

$$\begin{aligned} &\text{Amount (mg) of chlorpheniramine maleate} \\ &(\text{C}_{16}\text{H}_{19}\text{ClN}_2 \cdot \text{C}_4\text{H}_4\text{O}_4) \\ &= \text{amount (mg) of chlorpheniramine maleate} \\ &\text{for assay} \\ &\times \frac{A_T}{A_S} \times \frac{1}{50} \end{aligned}$$

**Containers and storage** Containers—Well-closed containers.